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ORIGINAL ARTICLE

Diagnostic Ultrasound Features and Outcome of Restrictive Foramen Ovale in Fetuses With Structurally Normal Hearts

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Abstract Intrauterine foramen ovale (FO) restriction in association with congenital heart disease (CHD) carries a poor prognosis. However, in the absence of CHD, the clinical importance of restrictive FO in the fetus is not well understood. We evaluated the antenatal prevalence, clinical presentation, diagnostic ultrasound features, and outcome of restrictive FO in fetuses without CHD. We reviewed the echocardiographic and clinical records of 23 fetuses diagnosed with a restrictive FO and structurally normal heart between 2001 and 2012. The atrial septum, dimensions of cardiac structures, left and right cardiac output and Doppler interrogation of cardiac flows were examined. The clinical outcomes of all fetuses with restrictive FO were analysed. Restrictive FO was identified in 23 of 1,682 (1.4 %) fetuses with no CHD. Enlarged right heart structures (100 %), hypermobile or redundant primum atrial septum (91 %), increased right-to-left ventricular cardiac output ratio (91 %), and posteriorly angulated ductus arteriosus (68 %) were the most common echocardiographic findings associated with this rare phenomenon. Additional noncardiac systemic abnormalities were identified in 13 (56 %) babies. Seven (30 %) neonates developed persistent pulmonary hypertension, and 7 infants died. Antenatal restrictive FO is an underrecognised entity despite being a common cause of right heart dilatation in the fetus. In the absence of CHD, restrictive FO is well tolerated antenatally, but its frequent association with noncardiac abnormalities and pulmonary hypertension in the neonate are noteworthy.

Keywords Fetus · Restriction · Foramen ovale · Right heart dilatation · Atrial septum · Aneurysm

Introduction

The fetal foramen ovale (FO) is a crescent-shaped intracardiac communication formed by the septum secundum on the right atrial side and the septum primum on the left

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side. The septum primum functions as the flap valve of the FO, allowing oxygen-rich blood arriving from the placenta to enter the left atrium. Fetal FO flow contributes approximately 76 % of the left-ventricular output. It must remain open during intrauterine life to maintain normal fetal circulation.

A restrictive FO in the presence of structural heart disease is associated with poor fetal and neonatal outcomes [5, 19, 23, 34, 35]. Premature closure of the fetal FO may lead to underdevelopment of the left ventricle, dilatation of the right heart structures, hydrops, and even intrauterine death [1, 5, 10, 19, 23, 26, 35]. However, restrictive FO occuring in the fetus with a normal heart is poorly understood [1, 10, 26]. To our knowledge, this is the first comprehensive survey of the prevalence, diagnostic ultrasound features, clinical characteristics, and outcome of restrictive FO in fetuses without congenital heart disease (CHD).

Materials and methods

We undertook a retrospective review of fetuses referred between 2001 and 2012 to the University Hospital of Wales Department of Fetal Cardiology for cardiac scanning. We searched our departmental database for right heart dilatation, atrial septal aneurysm, and restrictive FO. Those fetuses diagnosed with restrictive FO, atrial septal aneurysm, and dilated right heart constituted the subjects of this review. Those diagnosed with CHD or with no measurable objective criteria for FO restriction were excluded. All fetal cardiac examinations were performed by a single operator (O. U.).

Ethics Committee approval was not necessary because the review was retrospective, and the data were anonymised. The echocardiographic measurements were performed as part of routine clinical assessment. All scans were also anonymized.

Prerecorded ultrasound images of all fetuses with restrictive FO, atrial septal aneurysm, and dilated right heart were reviewed on an Echopac system (GE Ultrasound, Horten, Norway). Repeat measurements of fetal cardiac structures were performed at their maximal sizes, in appropriate scanning views, during either diastole or systole as previously described (Supplementary Fig. 1). The right- and left-ventricular diastolic dimensions were measured in four-chamber view just below the atrioventricular valves; right and left atrial widths and atrial septal lengths were measured in systole from the lateral walls of each atrium to the edge of secundum septum; dimensions of arteries and arterial valves were measured at end-systole using inner edge-to-inner edge method [5, 6, 15, 16, 21, 25, 31, 32]. Calculation of z-scores and cardiac output were performed off-line from the digitally stored images by two investigators (O. U., K. B.). These measurements were compared with the published normal data for the corresponding gestation [21, 22, 31, 32].

The prenatal appearance of the atrial septum and FO was considered normal (1) if the angle between the septum primum and septum secundum was between 30° and 50° (Supplementary Fig. 1) and, in addition, (2) if the flow across the FO was unrestricted with a triphasic Doppler pattern. The diameter of the FO was measured in the four-chamber and sagittal bicaval views (Supplementary Fig. 1). The diagnosis of restrictive FO was made on the basis of previously published criteria: (1) FO diameter <2.5 mm, (2) FO Doppler >40 cm/s, (3) FO/right atrial diameter <0.3, (4) FO/interatrial septum length <0.33, (5) FO/ascending aorta diameter <0.52 [6, 15, 27, 29, 36].

The FO flap was considered to be at risk of developing restriction when it appeared to be either aneurysmal (redundant or hypermobile) [29], fixed, or flat as previously described [10, 27, 36]. The presence of a dilated right heart, increased right-ventricular output, increased right-ventricular-to-left-ventricular output ratio, tricuspid regurgitation, and posteriorly angulated/large ductus arteriosus were considered to be supportive evidence for restrictive FO. Prenatal and postnatal clinical features and outcomes for each case were ascertained from the departmental database and from individual clinical hospital records.

Statistical Analysis

Data are presented as frequencies, mean ± SD or median and range as appropriate. χ^2 square or Fisher's exact tests (as appropriate) were used to assess statistical relations between categorical data. Sensitivity, specificity, and positive and negative predictive values were determined. Continuous variables were analysed using Mann–Whitney U test. Student t test was used to compare mean values. Statistical relationships were considered significant at $p < 0.05$.

Results

During the study period, 2324 fetuses were referred for cardiac scan. No structural heart defect was found in 1682 of them. Twenty-three had a restrictive FO, giving a prevalence of 1.4 % among this highly selected cohort. At the time of diagnosis of restrictive FO, the mean maternal age was 30.9 ± 6.3 years (range 20–44), and the mean gestational age was 33.0 ± 3.9 weeks (range 25–38).

Right heart dilatation was noted in 190 (8 %) fetuses, and 85 of these had structurally normal hearts. There were 149 (6 %) fetuses with atrial septal aneurysm; of these, 103 had no CHD. Forty fetuses with an atrial septal aneurysm

and a structurally normal heart had a dilated right ventricle. Hypermobile or redundant primum septum was evident in 21 fetuses, and a flat septum was documented in 2 fetuses. The prevalence of restrictive FO was 22 % among fetuses with an atrial septal aneurysm and 27 % among those exhibiting right heart dilatation without any CHD. Restrictive FO alone was the most common cause (26 %) of fetal right heart dilatation in our normal cohort (Supplementary Fig. 2). Table 1 lists the characteristics of all cases with restrictive FO. Twelve patients had fetal–maternal risk factors such as diabetes, oligohydramnios, polyhydramnios, increased placental resistance, and intrauterine growth restriction (IUGR).

The most common abnormalities detected by echocardiography in fetuses with restrictive FO are listed in Table 2. Enlarged right heart structures (100 %), a hypermobile or redundant atrial septum (91 %), and a posteriorly angulated ductus arteriosus (68 %) were the most common features (Fig. 1). Hypermobile primum septum was diagnosed in 13 fetuses with restrictive FO; this feature was seen in only 7 fetuses with no restriction. In the identification of restrictive FO, the finding of a hypermobile septum had a sensitivity of 56 % and a specificity of 92 % with a positive predictive value of 65 % and a negative predictive value of 89 % ($p < 0.001$). We encountered a posteriorly angulated ductus arteriosus (sagittal view) in 4 fetuses without restrictive FO compared with 15 fetuses with restrictive FO. Thus, posterior angulation of the ductus arteriosus had a sensitivity of 60 % and a specificity of 96 % with a positive predictive value of 79 % and a negative predictive value of 90 % for restrictive FO ($p < 0.001$). No restrictive ductus arteriosus was seen during the study period.

FO Doppler velocity was $\geq$0.4 m/s in 20 fetuses. The Doppler velocity of the FO could not be obtained in 3 cases. FO restriction was diagnosed between 26 and 38 weeks gestation (mean 33 $\pm$ 4). Complete closure of the FO did not occur in any of the fetuses, and the pulmonary venous Doppler pattern was invariably normal.

Right-ventricular output was substantially increased in 21 of the fetuses with FO restriction compared with those showing right heart dilatation without FO restriction (mean 0.75 vs. 0.59, $p < 0.002$) at the corresponding gestational period [22]. The mean ratio of right to left cardiac output was 3.42 in 21 fetuses, which is markedly greater (>2 z-score) than the reported normal value of 1.42 [22]. In 2 cases, cardiac output could not be calculated owing to poor-quality digital images. However, the discrepancy between right- and left-ventricular sizes was so striking that the initial diagnosis had been hypoplastic left ventricle in both of these fetuses (Fig. 1).

Outcomes of the fetuses with restrictive FO are shown in Fig. 2. Thirteen (56 %) were found to have at least 1 additional noncardiac problem either antenatally or postnatally. In 21 babies, the appearance of atrial septal aneurysm resolved with complete closure of the FO; however, in one infant a small secundum atrial septal defect developed. Moderate or severe tricuspid regurgitation (Supplementary Video 1) was detected in 6 fetuses (peak velocities 2.7–4.5 m/s). Eight fetuses exhibited irregular heart rhythm at presentation. Two fetuses with supraventricular tachycardia required treatment, and the arrhythmia resolved in both cases. No fetal death was directly attributable to restriction of the FO.

Seven neonates (30 %) developed persistent pulmonary hypertension. Of these, three required intensive care treatment. In the remaining four infants, pulmonary hypertension resolved on low-flow oxygen. One preterm baby died after birth owing to a combination of respiratory problems, cardiac failure, and severe pulmonary hypertension. A second infant died at 10 months from chronic renal failure, pulmonary hypertension, and respiratory issues due to Menkes disease.

Discussion

Our study provides the most comprehensive information to date on the diagnostic and clinical features of isolated restrictive FO in fetuses with normal hearts. Antenatal restriction of the FO is an underrecognised but frequent (26 %) cause of right heart dilatation. Our study shows that redundant/hypermobile primum atrial septum and posteriorly angulated ductus arteriosus are the most common echocardiographic findings associated with restrictive FO. These findings enhance our ability to predict FO restriction in fetal life, defining the clinical spectrum of this “not so benign” entity, which has associations with other pathologies and persistent pulmonary hypertension in the neonate.

Neither in our experience nor in that of others has there been strong evidence to suggest that the FO becomes restrictive toward term in normal fetuses [6, 15, 27, 31, 32]. The fetal FO grows progressively until 30 weeks gestation then continues to enlarge at a slower rate until term [15]. The diameter of the FO, and the ratios of FO to the atrial septum and FO to the ascending aorta diameter, provide objective evidence for FO patency. Echocardiography parameters, such as ratios of FO-to-aortic root diameter (<0.66), FO-to-atrial septal length (<0.33), and FO-to-right atrial diameter (<0.3), have been proposed as surrogate markers for FO restriction [30, 31]. Because the right atrium is significantly dilated in restrictive FO, the ratio of the FO to the right atrial diameter would be misleading. In our study, all 23 patients had an FO diameter of <3.5 mm, a FO-to-atrial septal length ratio of <0.33, and an FO-to-

Table 1 The clinical characteristics of mothers and fetuses

Case no.	Referral reason	Maternal risk factors	Atrial septum	Ductus arteriosus	Neonatal echocardiography	Additional findings	Outcome
1	Large right ventricle	Oligohydramnios, smoking	Redundant, hypermobile	Nonrestrictive posterior	Persistent pulmonary hypertension	None	Alive
2	Large right ventricle, arrhythmia	Oligohydramnios	Flat	Nonrestrictive posterior	Impaired left-ventricular function, right ventricular hypertrophy	None	Alive
3	Large right ventricle	Smoking, ANA (+)	Redundant, hypermobile	Nonrestrictive anterior	Normal	None	Alive
4	Large right ventricle	Smoking	Redundant	Nonrestrictive posterior	Normal	None	Alive
5	Large right ventricle, arrhythmia	IUGR, increased placental resistance	Flat	Nonrestrictive posterior	Persistent pulmonary hypertension, impaired right and left ventricular function, tricuspid valve dysplasia	Alstrom syndrome, hypospadias, WPW	Alive
6	Large right ventricle	None	Redundant, hypermobile	Nonrestrictive posterior	Normal	None	Alive
7	Large right ventricle	Smoking	Redundant	Nonrestrictive anterior	Normal	None	Alive
8	Large right ventricle, arrhythmia	Oligohydramnios, increased placental resistance	Redundant	Nonrestrictive posterior	Normal	None	Alive
9	Large right ventricle	Preeclampsia	Redundant, hypermobile	Nonrestrictive posterior	Persistent pulmonary hypertension	Coeliac disease, hypothyroidism, short stature	Alive
10	Small left ventricle	Oligohydramnios, hypothyroidism	Redundant, hypermobile	Nonrestrictive posterior	Normal	None	Alive
11	Large right ventricle	Increased placental resistance, smoking	Redundant, hypermobile	Nonrestrictive posterior	Normal	None	Alive
12	Large right ventricle, arrhythmia	None	Redundant, hypermobile	Nonrestrictive anterior	Normal	None	Alive
13	Large right ventricle	Guillain–Barre, SSRI	Redundant	Nonrestrictive anterior	Normal	None	Alive
14	Large right ventricle	None	Redundant, hypermobile	Nonrestrictive posterior	Normal	None	Alive
15	Large right ventricle, arrhythmia	Oligohydramnios, smoking	Redundant	Nonrestrictive posterior	Normal	Ureter obstruction, hydronephrosis	Alive
16	Large right ventricle	None	Redundant	Nonrestrictive posterior	Normal	Cleft lip palate	Alive
17	Large right ventricle	Increased nuchal translucency	Redundant, hypermobile	Nonrestrictive posterior	Normal	Down syndrome	Alive

Table 1 continued

Case no.	Referral reason	Maternal risk factors	Atrial septum	Ductus arteriosus	Neonatal echocardiography	Additional findings	Outcome
18	Large right ventricle	Insulin dependent diabetes, hyperthyroidism, smoking	Redundant	Nonrestrictive posterior	Persistent pulmonary hypertension, impaired biventricular function	VACTERL syndrome	Died at birth
19	Large right ventricle	Parvovirus infection, fetal anaemia, hydrops	Redundant, hypermobile	Nonrestrictive anterior	Persistent pulmonary hypertension	Hypospadias	Alive
20	Large right ventricle	None	Redundant	Nonrestrictive posterior	Normal	Menkes syndrome, posterior urethral valve, hydronephrosis, bradycardia	Died at 10 months
21	Large right ventricle, arrhythmia	Atrial flutter	Redundant, hypermobile	Nonrestrictive anterior	Normal	None	Alive
22	Large right ventricle	Gestational diabetes, SSRI	Redundant, hypermobile	Nonrestrictive anterior	Large patent ductus arteriosus	None	PDA device closure
23	Large right ventricle, arrhythmia	Polyhydramnios, smoking, SSRI	Redundant, hypermobile	Nonrestrictive anterior	Persistent pulmonary hypertension, right ventricular hypertrophy, tricuspid valve dysplasia	None	Alive

aortic root diameter ratio of <0.6. We recommend using the atrial septal length criterion when diagnosing restrictive FO in the fetus.

Doppler assessment of the atrial septum for the diagnosis of FO restriction is challenging because of its complex structure [5, 19, 29, 34]. We could obtain increased FO Doppler velocity measurements in 20 fetuses with restrictive FO; in the remaining three cases other objective supportive evidence for FO restriction could be showed. All of our patients met at least one objective criterion for FO restriction. The maxium right-to-left Doppler velocity of the FO in normal fetuses is reported to be <0.4 m/s (mean 0.23), and the left-to-right flow velocity is <0.2 m/s (mean 0.14) [28, 37]. In this study, 86 % of patients with restrictive FO had a maximum right-to-left FO Doppler velocity ≥0.4 m/s (mean 0.60 ± 0.16). Rasanen et al. [30] found that fetal FO blood flow decreased from 34 % of combined cardiac output at 20 weeks to 18 % at 30 weeks, whereas the proportions of FO blood flow and pulmonary blood flow remained unchanged between 30 and 38 weeks. Similarly, Mielke and Benda [22] showed that median FO blood flow provided 33 % of combined cardiac output. As venous return to the right ventricle gradually increases in the third trimester, in normal fetuses the right-to-left ventricle ratio increases from 1.05 at 28 weeks to 1.19 at 40 weeks of gestation [15, 31, 32]. In normal fetuses, mean ratio for right-to-left cardiac output of 1.42 does not vary with gestational age, thus confirming antenatal right-ventricular dominance [22]. In our study, all 23 restrictive FO patients had marked enlargement of the right heart chambers with a mean right-to-left ventricle ratio of 1.56 ± 0.2. The presence of restrictive FO was further supported by a significantly increased right-to-left ventricular output ratio of 3.42 ± 1.5 (range 1.88–7.99). This was significantly greater than the reported normal value of 1.42 ($p < 0.002$) [22]. In the absence of other causes of right heart dilatation, this objective evidence of increased right-ventricular output supports the notion that restrictive FO increases shunting of blood into the right ventricle

Premature restriction of the fetal FO either occurs due to a primary maldevelopment of the septum primum or as a haemodynamic consequence of increased left atrial pressure [1, 11]. The presence of an atrial septal aneurysm in the context of restrictive FO has been mentioned in a few case reports [1, 10]. Maeno et al. [19] suggested that an atrial septal aneurysm should be considered indicative of potential FO restriction. Likewise, Punn and Silverman [29] proposed a similar mechanism for fetuses exhibiting a hypermobile septum primum and postnatal FO restriction in the context of transposition of the great arteries. A hypermobile septum primum flap may cause FO restriction by thickening and abutting against the septum secundum

Table 2 The most common abnormalities detected on echocardiography

Examined cardiac structure	Patients	%	Range	Mean ± SD
Foramen ovale				
FO diameter ≤2.5 mm	17	74	1.3–3.0	2.21 ± 0.43
FO Doppler ≥0.4 m/s	20	87	0.4–0.92	0.60 ± 0.16
Redundant atrial septum	21	91		
Hypermobile atrial septum	13	57		
FO/right atrium ratio <0.3	23	100	0.06–0.16	0.11 ± 0.03
FO/aorta size <0.52	23	100	0.22–0.52	0.36 ± 0.09
FO/atrial septum length <0.33	23	100	0.081–0.2	0.14 ± 0.04
Right heart				
Dilated right atrium	23	100		
Dilated right ventricle *z*-score >2	10	43	−0.35 ± 4.91	1.92 ± 1.5
Right/left ventricle size >1.2	23	100	1.23–2.12	1.57 ± 0.21
Moderate tricuspid regurgitation	12	52		
Cardiac output				
Right-ventricular output >0.65	21	91	0.65–0.89	0.75 ± 0.07
Right-/left-ventricular output >1.42	21	91	1.88–7.99	3.42 ± 1.5
Pulmonary artery				
Pulmonary/aorta size >1.2	23	100	1.2–2.07	1.55 ± 0.27
Ductus arteriosus				
Posteriorly angulated ductus	15	68		
Nonrestrictive anterior ductus	8	35		
Aortic isthmus				
Isthmus-to-ductus ratio <0.74	17	74	1.02–2.8	1.69 ± 0.38

late in gestation [29]. Obstructed fetal FO and atrial septal aneurysm have also been linked to fetal cardiac rhythm disturbances [2]. Conversely, supraventricular tachycardia *per se* may act as a stimulant for the development of atrial septal aneurysm [2, 9, 28, 37]. In our study, heart rhythm abnormality in association with restrictive FO was present in eight patients (34 %), and in one case the restriction became evident only after resolution of intermittent supraventricular tachycardia. We concur with the previous suggestions that a redundant or hypermobile atrial septum is likely to play a major role in the early restriction of the FO; therefore, such an association should not be considered coincidental. A redundant atrial septal aneurysm was identified in 6 % of all patients scanned but was present in the majority (91 %) of those with restrictive FO. Restrictive FO occurred in only 22 % of all our cases with atrial septal aneurysm, but it is of note that 65 % of fetuses found to have a hypermobile atrial septum developed a restrictive FO ($p = 0.0007$).

The pathophysiological mechanisms of right heart dilatation may involve increased preload or afterload, but diagnosing the specific clinical aetiology of such changes requires the elimination of a long list of fetal and maternal conditions (Supplemental Table 1). Hornung et al. [12] reported on 43 fetuses with right heart dilatation but made no reference to the presence of atrial septal aneurysm or restrictive FO. Among their fetuses, 19 (44 %) had isolated right heart dilatation, and 9 (21 %) showed significant noncardiac anomalies. Significant noncardiac anomalies were also found to be common in our cohort with restrictive FO. Our study suggests that premature restriction of the FO should be considered among the main causes of right heart dilatation in the fetus (Supplementary Fig. 2). However, one must of course be mindful of other possible mechanisms and causes of right-ventricular dilatation (Supplementary Table 1) such as premature constriction of the ductus arteriosus [7], arteriovenous malformations, vein of Galen aneurysm, absent ductus venosus [18], and left diaphragmatic hernia [33]. None of our patients exhibited the previously mentioned structural pathologies to account for their right heart dilatation. Right heart prominence has also been shown to occur in fetuses with hypertrophic cardiomyopathy, ventricular septal hypertrophy secondary to maternal diabetes [28], IUGR [16, 37], and either increased placental resistance or placental dysfunction [9, 12, 28, 37]. Because we did encounter the last three of these pathologies in some of our cases, one could argue that they might have contributed to fetal right heart dilatation as much as a restrictive FO.

Mielke and Benda [21] suggested that neither kinking of the ductus arteriosus nor an S-shaped ductus were observed in normal fetuses in the sagittal plane; hence, a posteriorly

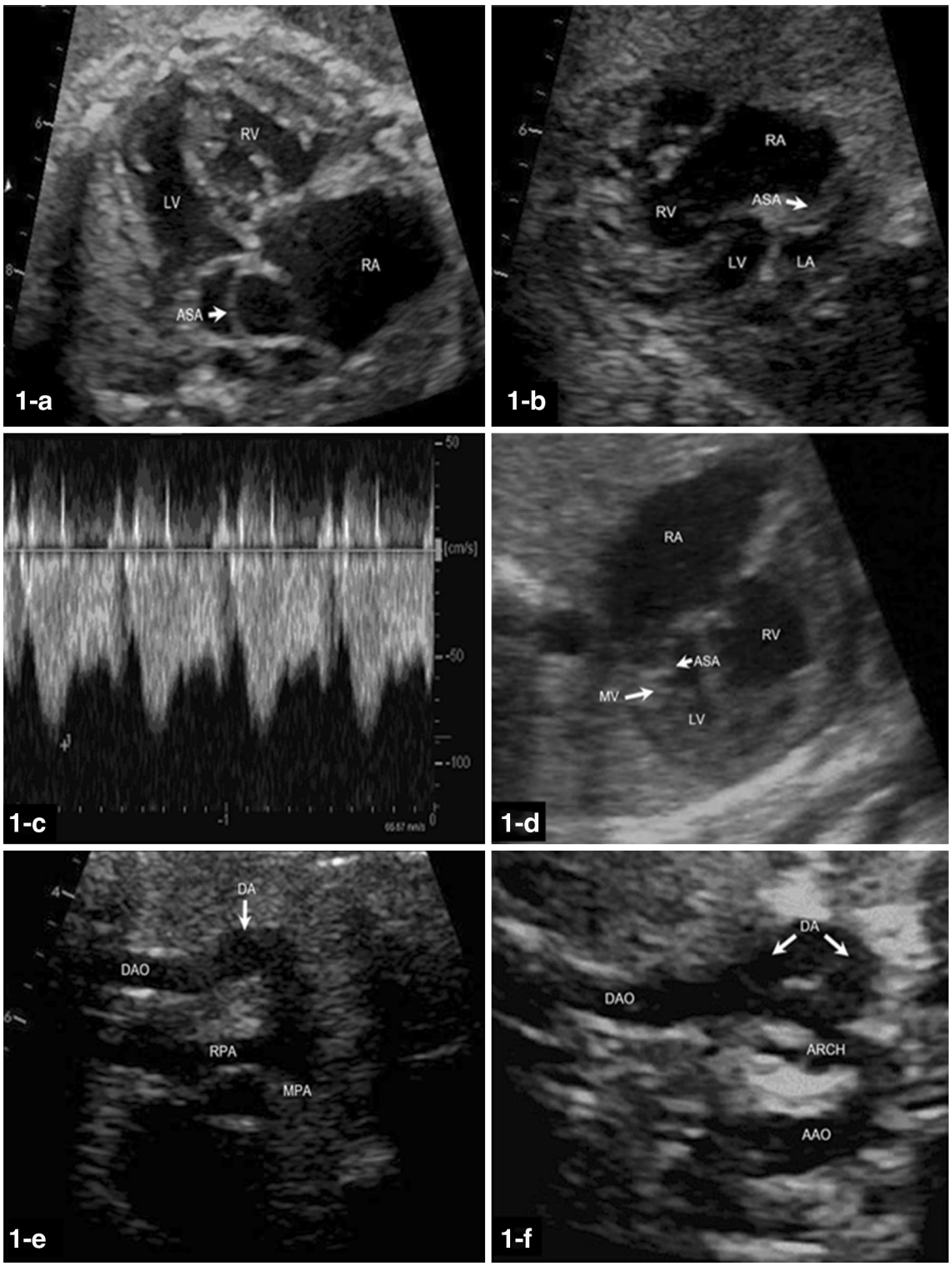

Fig. 1 Echocardiographic characteristics of fetuses with restrictive FO and normal heart. **a** Restrictive FO with aneurysmal/redundant atrial septum and dilated right heart chambers. **b** Flat atrial septum. **c** FO Doppler tracing shows an increase in FO velocity indicating significant restriction. **d** Atrial septal aneurysm prolapsing into the left-ventricular inflow and causing partial obstruction, which mimics common atrium and hypoplastic left heart syndrome. **e** Posteriorly angulated ductus arteriosus. **f** Overlapped images of aortic arch and posteriorly inserted ductus arteriosus

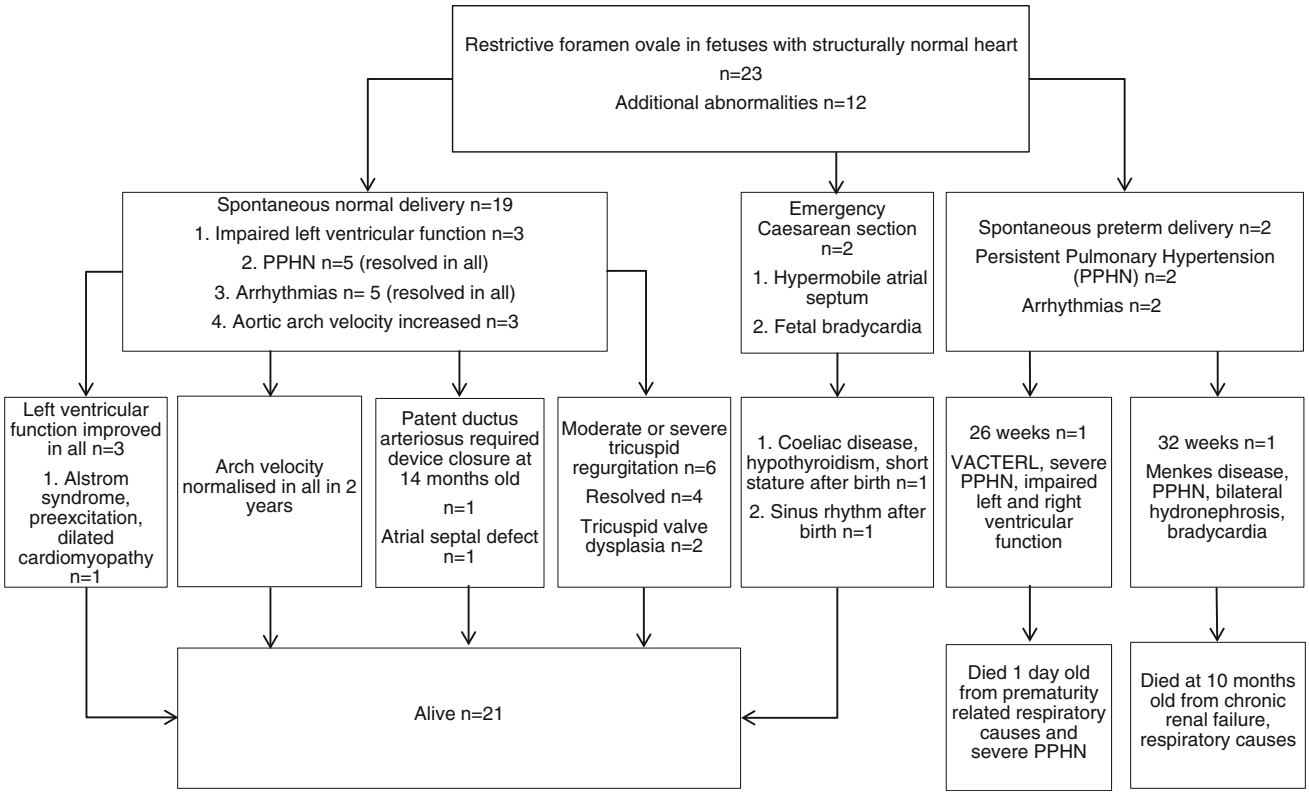

Fig. 2 Outcome of fetuses with restrictive FO and structurally normal heart

angulated (S-shaped) ductus arteriosus should not be considered a normal finding. Although we encountered a posteriorly angulated ductus arteriosus in four fetuses (0.2 %) without restrictive FO (all four of these had a redundant/hypermobile primum atrial septum), this feature was showed in 65 % of fetuses with restrictive FO ($p < 0.001$). Therefore, in our opinion, a posteriorly angulated ductus arteriosus (in the absence of ductal constriction) should be considered an important hallmark of restrictive FO. The mechanism underlying this altered anatomy may be that the attachment angle of the ductus arteriosus moves posteriorly as it transmits the increased right-ventricular volume into the descending aorta. In all of our cases, the diameter of the ductus arteriosus was large (mean 0.52 ± 0.1 cm), and Doppler velocity was normal with no increase in systolic or diastolic flow velocities; therefore, kinking or constriction of the arterial duct could be confidently excluded.

Some of our fetuses exhibited a relatively small left heart, severe tricuspid regurgitation (Supplementary Video 1), a small aortic isthmus, and an isthmus-to-ductus (I/D) ratio <1.74. These features are generally considered suggestive of left heart obstructive lesions [14, 20, 25]. Thirteen cases were referred to us on suspicion of coarctation of the aorta; in 2 fetuses, hypoplastic left heart was the initial diagnosis at the referring centre. As one might anticipate, 18 fetuses in our study showed an I/D ratio <0.74. Postnatally, none of these cases had significant coarctation of the aorta (requiring intervention or treatment), but all were proven to have a restrictive FO. According to the severity of FO restriction, a greater volume of systemic venous return is diverted into the right ventricle. Diminished flow from the FO into the left ventricle results in a smaller cavity size. Decreased downstream blood flow into the descending aorta further exacerbates an intrinsically small aortic isthmus.

Antenatal restriction or closure of the FO in structurally normal hearts may result in right-ventricle volume loading, severe tricuspid regurgitation, and increased systemic venous pressures, which may in turn lead to congestive cardiac failure, fetal hydrops, or even death [1, 3, 4, 10, 11, 17, 24, 26]. In our study, 3 newborns showed impaired left-ventricular function. Complete recovery of function occurred in 2 infants with treatment, but the left ventricle remained dilated in 1 child with Alström syndrome. Although there was no intrauterine death among fetuses with restrictive FO, the frequency of noncardiac abnormalities (in 12 babies) was striking. We suggest that the presence of FO restriction should alert the clinician to the possibility of other systemic abnormalities. In theory, premature closure of the fetal FO may increase the risk of subsequent persistent pulmonary hypertension in the

neonate (owing to decreased fetal pulmonary vascular resistance in response to more oxygen-rich blood being shifted to the pulmonary arteries). In contrast, some investigators have shown the opposite, i.e., that neonates with restrictive FO and severe pulmonary hypertension had a faster decrease in pulmonary artery pressure compared with those who had a nonrestrictive FO [8, 13]. However, our finding of persistent pulmonary hypertension occurring in 7 (30 %) of 23 infants postnatally is at odds with the findings of those studies. In our cohort, 3 neonates required intensive care treatment with pulmonary vasodilators and mechanical ventilation, but only 1 responded to treatment.

Limitations of the Study

We acknowledge the retrospective nature of this study. Our institution is the main tertiary referral center for South Wales, and we see only the most serious abnormalities. Due to referral bias, our study could not capture all fetal cases with atrial septal aneurysm or right heart dilatation. Restrictive FO is a rare diagnosis, and owing to the limited number of patients considered in this study, prescriptive guidelines cannot be derived from our results. Prospective studies on an unselected cohort would be required to confirm the true incidence and aetiological mechanism of FO restriction as well as its relationship with hypermobile primum atrial septum.

Conclusion

Premature restriction of the FO is a rare phenomenon in fetuses with structurally normal hearts. Although under-recognised, it is a relatively common cause of fetal right heart dilatation. A finding of fetal right heart dilatation associated with a hypermobile atrial septal aneurysm and a posteriorly angulated ductus arteriosus should raise suspicion of restrictive FO.

As long as the fetus remains haemodynamically stable without left-ventricular inflow obstruction, sustained tachycardia, or right heart failure, the prognosis of restrictive FO is good, and pregnancy should be allowed to continue until term with close monitoring. However, owing to the frequent association of restrictive FO with noncardiac abnormalities and persistent pulmonary hypertension in the neonate, we recommend delivery at a unit with appropriate neonatal support and detailed ultrasound examination to exclude other systemic abnormalities in the fetus and newborn baby.

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